SUMMARY OF SAFETY AND EFFECTIVENESS

JAN - 6 2012

Assigned 510(k) Number

The assigned 510(k) number is: **k112523**.

Sponsor Name and Address

Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591
(Office) 914-524-3270
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Contact

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Device Name

Trade name:	IMMULITE® 2000 3gAllergy™ Specific IgE Assay
Classification:	Class II
Classification Names:	Radioallergosorbent (RAST) Immunological Test System
Regulation Number:	866.5750
Product Code:	DHB
Catalog Numbers:	L2KUN6 (600 tests)

Description of Device

IMMULITE® 2000 3gAllergy™ Specific IgE is a solid-phase, two-step, chemiluminescent immunoassay that exploits liquid phase kinetics in a bead format.[1,2]

(U.S. Patent No. 4,778,751) It represents a significant advance over conventional methods relying on allergens attached to a solid-phase support, such as a paper disk.

The allergens are covalently bound to a soluble polymer/co-polymer matrix, which in turn is labeled with a ligand. The use of an amino acid co-polymer amplifies the amount of allergen that the matrix can support.

Incubation Cycles: 2 × 30 minutes.

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[1] El Shami AS, Alaba O. Liquid-phase *in vitro* allergen-specific IgE assay with *in situ* immobilization. Adv Biosci 1989;74:191–201.

[2] Alaba O, El Shami AS. Evaluation of non-specific IgE binding: comparison of two *in vitro* allergen assays. Adv Biosci 1989;74:203–14.

Indications for Use

For *in vitro* diagnostic use with the IMMULITE® 2000 Analyzer — for the quantitative measurement of allergen-specific IgE in human serum, as an aid in the clinical diagnosis of IgE-mediated allergic disorders. The test results are to be used in conjunction with clinical findings and other laboratory tests.

Establishment Information

IMMULITE® 2000 3gAllergy Specific IgE assay is manufactured by Siemens Healthcare Diagnostics Inc. at the following locations:

Siemens Healthcare Diagnostics Products, LTD
Glyn Rhonwy, Llanberis, Gwynedd, LL55 4EL, United Kingdom
Telephone Number: 44 1286 878187 188408
Fax Number: 44 1286 87818718
FDA Establishment Registration: 9610633

Siemens Healthcare Diagnostics Inc.
5210 Pacific Concourse Drive
Los Angeles, CA 90045-8200
Telephone Number: (310)-645-8200
Fax Number: (310)-645-9999
FDA Establishment Registration: 3005250747

Predicate

The purpose of this 510(k) submission is for clearance of five additional specific allergens, named in the table below, to be used with the IMMULITE® 2000 3gAllergy™ Specific IgE assay on the IMMULITE® 2000 analyzer.

1	A482 (Native Ole e 1)	**4**	E220 (Cat Serum Albumin , Fel d 2)
2	A753 (Native Art v 1)	**5**	E221 (Dog Serum Albumin , Can f 3)
3	A89 (Native Bet v 1)		

FDA clearance was previously obtained for the assay kit and 106 specific allergens (K093987, K100910 and K101572).

Please note that the FDA clearances indicated above were in the name of Diagnostic Products Corporation which was acquired by Siemens Medical Solutions Diagnostics in July 2006. Siemens Medical Solutions Diagnostics was renamed Siemens Healthcare Diagnostics Inc. on January 1, 2008.

Similarities		
Description Item	**IMMULITE Device**	**Predicate Device**
Indication for Use	For *in vitro* diagnostic use with the IMMULITE® 2000 Analyzer — for the quantitative measurement of allergen-specific IgE in human serum, as an aid in the clinical diagnosis of IgE-mediated allergic disorders. The test results are to be used in conjunction with clinical findings and other laboratory tests.	Same
Number of Calibrators	Eight	Same
Sample Matrix	Serum	Same
Antibody	Monoclonal murine anti-human IgE conjugated to alkaline phosphatase	Same
Basic Principle	Chemiluminescent Immunoassay	Same
Sample Volume	50 µl	Same
Process Time	65 minutes	Same
Incubation Temperature	37°C	Same
Differences		
Modifications	Allergenic proteins purified from native sources	Native whole allergens

Precision

Precision studies were performed in accordance with Clinical Laboratory Standard Institute (CLSI) guidance: *Evaluation of Precision Performance of Quantitative Methods; Approved Guideline-Second Edition.* CLSI document EP5-A2 (ISBN 1-56238-542-9). CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2004, assaying two aliquots of each test sample in two runs per day on 20 different days (Positives 1-3). Additional studies for Positives 4 and 5 were run with two runs per day over 20 days. Analysis of variance was used to estimate the within-run and total precision.

Three allergen lots were tested using three positive samples and one negative sample. Intra-assay and inter-assay precision for the positive samples were evaluated by calculating the kU/L dose percent coefficients of variation (%CV) for each positive sample. Non-specific binding (NSB) was monitored by testing the negative control sample. Representative precision claims for each allergen tested are presented below:

Precision statistics using instrument I3474 and I3476 for the 5 individual allergens, noting allergen lot used are presented in the following tables:

Allergen Precision Claims

Sample	N	Within-Run			Total	
		Mean (kU/L)	SD (kU/L)	CV %	SD (kU/L)	CV %
Allergen = nOle e 1, Lot 201						
Positive #1	80	0.50	0.027	5.46	0.030	5.98
Positive #2	80	1.91	0.119	6.23	0.134	7.03
Positive #3	80	17.34	0.686	3.95	1.013	5.85
Allergen = nOle e 1, Lot 202						
Positive #1	80	0.52	0.028	5.48	0.033	6.38
Positive #2	80	1.97	0.095	4.84	0.117	5.96
Positive #3	80	17.80	0.702	3.94	1.068	6.00
Allergen = nOle e 1, Lot 203						
Positive #1	80	0.51	0.027	5.18	0.035	6.90
Positive #2	80	2.00	0.111	5.55	0.139	6.93
Positive #3	80	17.82	0.907	5.09	1.156	6.48

Sample	N	Mean	Within-Run SD	Within-Run CV	Total SD	Total CV
		(kU/L)	(kU/L)	%	(kU/L)	%
Allergen = nArt v 1, Lot 201						
Positive #1	80	1.28	0.040	3.15	0.066	5.15
Positive #2	80	5.13	0.196	3.83	0.288	5.61
Positive #3	80	52.54	1.676	3.19	2.671	5.08
Positive #4	80	0.44	0.015	3.41	0.021	4.67
Positive #5	80	0.46	0.018	3.94	0.033	7.10
Allergen = nArt v 1, Lot 202						
Positive #1	80	1.28	0.137	10.65	0.144	11.25
Positive #2	80	5.16	0.227	4.39	0.293	5.68
Positive #3	80	52.43	1.862	3.55	2.873	5.48
Positive #4	80	0.43	0.017	4.04	0.028	6.49
Positive #5	80	0.46	0.012	2.72	0.032	7.02
Allergen = nArt v 1, Lot 203						
Positive #1*	80	1.53	1.697	111.20	1.710	112.08
Positive #1**	78	1.32	0.156	11.67	0.144	10.87
Positive #2	80	5.10	0.225	4.40	0.307	6.02
Positive #3	80	52.13	2.253	4.32	2.839	5.45
Positive #4	80	0.43	0.015	3.51	0.026	5.94
Positive #5	80	0.47	0.016	3.35	0.033	7.03

*Two Outliers detected (Day 12, Run 2, Rep Number 2) (Day: 15, Run: 1, Rep Number 1)

**No outliers used in calculation

			Within-Run		Total	
Sample	N	Mean	SD	CV	SD	CV
		(kU/L)	(kU/L)	%	(kU/L)	%
Allergen = Dog Serum Albumin (Can f 3), Lot 201						
Positive #1	80	47.84	1.056	2.21	1.979	4.14
Positive #2	80	23.10	0.950	4.11	1.170	5.07
Positive #3	80	0.87	0.024	2.81	0.064	7.35
Positive #4	80	0.44	0.015	3.50	0.040	9.17
Positive #5	80	0.46	0.025	5.46	0.034	7.24
Allergen = Dog Serum Albumin (Can f 3), Lot 202						
Positive #1	80	48.19	6.043	12.54	6.252	12.97
Positive #2	79	23.05	0.751	3.26	1.041	4.52
Positive #3	80	0.87	0.028	3.21	0.057	6.54
Positive #4	80	0.44	0.015	3.35	0.045	10.19
Positive #5	80	0.48	0.020	4.09	0.029	6.01
Allergen = Dog Serum Albumin (Can f 3), Lot 203						
Positive #1	80	48.83	1.248	2.55	2.119	4.34
Positive #2	80	22.97	0.809	3.52	1.291	5.62
Positive #3	80	0.84	0.027	3.28	0.065	7.78
Positive #4	80	0.44	0.016	3.58	0.044	9.88
Positive #5	80	0.48	0.020	4.23	0.034	7.11

			Within-Run		Total	
Sample	N	Mean	SD	CV	SD	CV
		(kU/L)	(kU/L)	%	(kU/L)	%
Allergen = nBet v 1, Lot 201						
Positive #1	80	2.42	0.102	4.22	0.103	4.23
Positive #2	80	9.24	0.304	3.29	0.352	3.81
Positive #3	80	23.78	0.898	3.77	1.038	4.36
Positive #4	80	0.39	0.020	5.16	0.024	6.28
Positive #5	80	0.41	0.018	4.34	0.025	6.17
Allergen = nBet v 1, Lot 202						
Positive #1	80	2.42	0.104	4.30	0.107	4.43
Positive #2	80	9.25	0.309	3.34	0.381	4.11
Positive #3	80	23.78	0.717	3.02	0.987	4.15
Positive #4	80	0.38	0.015	4.00	0.024	6.28
Positive #5	80	0.41	0.017	4.18	0.028	6.83
Allergen = nBet v 1, Lot 203						
Positive #1	80	2.36	0.095	4.04	0.109	4.63
Positive #2	80	9.09	0.284	3.12	0.344	3.78
Positive #3	80	22.94	0.724	3.16	0.828	3.61
Positive #4	80	0.38	0.015	3.86	0.020	5.38
Positive #5	80	0.41	0.015	3.77	0.030	7.32

		Within-Run			Total	
Sample	N	Mean	SD	CV	SD	CV
		(kU/L)	(kU/L)	%	(kU/L)	%
Allergen = Cat Serum Albumin (Fel d 2), Lot 201						
Positive #1	80	0.91	0.031	3.41	0.055	6.03
Positive #2	80	36.38	1.173	3.22	1.365	3.75
Positive #3	80	45.81	2.032	4.44	2.032	4.44
Positive #4	80	0.36	0.013	3.58	0.021	5.80
Positive #5	80	0.38	0.014	3.74	0.023	6.12
Allergen = Cat Serum Albumin (Fel d 2), Lot 203						
Positive #1	80	0.92	0.027	2.94	0.063	6.91
Positive #2	80	35.86	0.853	2.38	1.046	2.92
Positive #3	80	44.62	1.260	2.82	1.556	3.49
Positive #4	80	0.36	0.012	3.47	0.026	7.22
Positive #5	80	0.38	0.018	4.70	0.028	7.25
Allergen = Cat Serum Albumin (Fel d 2), Lot 204						
Positive #1	80	0.97	0.027	2.77	0.067	6.93
Positive #2	80	36.41	0.942	2.59	1.125	3.09
Positive #3	80	45.38	1.362	3.00	1.685	3.71
Positive #4	80	0.35	0.018	5.18	0.023	6.36
Positive #5	80	0.38	0.019	4.98	0.025	6.68

Lot-to-Lot variability is summarized in the following tables for each of the 5 allergens.

			Within-Run		Total	
Sample	N	Mean (kU/L)	SD (kU/L)	CV %	SD (kU/L)	CV %
Allergen = nOle e 1 (Lots 201, 202, 203)						
Positive #1	240	0.51	0.030	5.88	0.034	6.67
Positive #2	240	1.96	0.115	5.87	0.136	6.94
Positive #3	240	17.65	0.863	4.89	1.075	6.09
Allergen = nArt v 1 (Lots 201, 202, 203)						
Positive #1*	240	1.36	0.992	72.94	0.999	73.46
Positive #1**	239	1.30	0.134	10.31	0.151	11.62
Positive #2	240	5.13	0.214	4.17	0.297	5.79
Positive #3	240	52.37	1.905	3.64	2.737	5.23
Positive #4	240	0.44	0.016	3.65	0.025	5.75
Positive #5	240	0.46	0.016	3.46	0.033	7.06
***Outlier Detected (Day: 12, Run: 2, Rep Number: 2)**						
****No outliers used in calculation**						
Allergen = Dog Serum Albumin (Can f 3) (Lots 201, 202, 203)						
Positive #1	240	48.29	3.571	7.39	3.825	7.92
Positive #2	240	23.04	0.829	3.60	1.146	4.97
Positive #3	240	0.86	0.058	6.74	0.063	7.33
Positive #4	240	0.44	0.015	3.44	0.042	9.61
Positive #5	240	0.48	0.022	4.67	0.032	6.79

			Within-Run		Total	
Sample	N	Mean	SD	CV	SD	CV
		(kU/L)	(kU/L)	%	(kU/L)	%
Allergen = nBet v 1 (Lots 201, 202, 203)						
Positive #1	240	2.40	0.101	4.19	0.108	4.49
Positive #2	240	9.19	0.299	3.25	0.353	3.84
Positive #3	240	23.50	0.784	3.34	0.998	4.25
Positive #4	240	0.38	0.017	4.41	0.022	5.85
Positive #5	240	0.41	0.017	4.08	0.028	6.76
Allergen = Cat Serum Albumin, Fel d 2 (Lots 201, 203, 204)						
Positive #1	240	0.93	0.028	3.04	0.066	7.12
Positive #2	240	36.22	0.988	2.76	1.181	3.26
Positive #3	240	45.27	1.588	3.51	1.778	3.93
Positive #4	240	0.36	0.015	4.11	0.023	6.43
Positive #5	240	0.38	0.017	4.44	0.025	6.68

Precision of nOle e 1, nArt v 1, Dog Serum Albumin (Can f 3), nBet v 1, and Cat Serum Albumin (Fel d 2) meet the criteria for acceptable intra- assay precision, inter- assay precision, and lot-to-lot precision. Intra-assay variability is less than 15% for all allergen lots, inter-assay precision is less than 15% for all allergen lots, and lot-to-lot precision is less than 20% for all 5 allergens. The average negative control remained negative (< 0.10 kU/L) throughout precision testing on all allergens.

Linearity

For each allergen, two samples were diluted in 2-fold serial dilution to five (5) levels. The undiluted (neat) and diluted samples were tested with the specific allergen to demonstrate linearity at concentrations within the assay limits. Regression statistics for each allergen comparing observed to expected data are presented below.

Linearity

Allergen	Regression Equation	N	Slope 95% CI	Intercept 95% CI	R	Range Tested (kU/L)
nOle e 1	y = 0.997x + 0.0993	11	0.974 - 1.020	0.0234 - 0.1753	0.999	0.14 - 9.43
nArt v 1	y = 1.004x + 0.3830	12	0.972 - 1.035	-0.1692 - 0.9352	0.998	1.11 - 40.00
Dog Serum Albumin	y = 0.999x - 0.0832	12	0.986 - 1.012	-0.1906 - 0.0242	1.000	0.31 - 23.15
nBet v 1	y = 0.994x + 0.1429	12	0.972 - 1.016	-0.0569 - 0.3428	0.999	0.60 - 22.24
Cat Serum Albumin	y = 0.975x + 0.0230	12	0.928 - 1.023	-0.6815 - 0.7275	0.995	0.52 - 42.40

Specificity (Inhibition) Studies

Specificity of each allergen was verified through competitive inhibition testing using a single serum sample or pool of sera. A negative sample was used to measure the background response.

To initiate the inhibition experiment, 70 µL of undiluted and 3-4 levels of 5-fold serially diluted inhibitor extract were mixed with 250 µL of sample or pool to achieve final inhibitor concentrations of 218.75, 43.75, 8.75, 1.75, 0.35, 0.08, 0.07, 0.02, 0.01, 0.003 µg/mL. This mixture was incubated at room temperature (15-28 °C) for 1 hour allowing the immunological reaction to occur. Each sample mixture containing the inhibitor extract and the appropriate controls was assayed with 1 lot of each allergen. The percent (%) inhibition was calculated according to the following formula:

$$\left[\frac{(\text{Response of pos. control}_{(\text{pos. sample} - \text{neg. sample})} - \text{sample response with inhibitor extract})}{(\text{Response of pos. control}_{(\text{pos. sample} - \text{neg. sample})})}\right] \times 100$$

The inhibition plots demonstrate that the allergens tested are inhibited by the relevant inhibitor extract in a concentration dependent fashion. Also, the target % inhibition of 50% for the highest inhibitor concentration tested was met. These results indicate specificity of Native Ole e 1, Native Art v 1, Dog Serum Albumin, (Can f 3), Native Bet v 1 and Cat Serum Albumin, (Fel d 2) allergens.

Inhibition Using Negative Controls

Additional inhibitions studies were conducted to show that the specific allergens are not cross-reacting to unrelated allergens.

Procedures were followed according to CLSI ILA20-A2. Testing was performed using one positive sample with three unrelated allergen extracts at 1 mg/ml. A negative sample was used to measure the background response. Inhibition for each allergen with three unrelated extracts did not generate any significant inhibition. These results indicate specificity of nOle e 1, nArt v 1, Dog Serum Albumin (Can f 3), nBet v 1, and Cat Serum Albumin (Fel d 2) allergens.

Clinical Performance Studies

Clinical performance was demonstrated by testing serum samples against specific allergens from clinically diagnosed atopic and non-atopic individuals. Allergen-specific testing was obtained using the IMMULITE® 2000 3gAllergy™ assay.

Data summary agreement of the IMMULITE® 2000 3gAllergy™ results to clinical data is presented in the table below.

Clinical Diagnosis Data			
IMMULITE® 2000 Analyzer	**Clinical**	**Normal**	**Total**
Positive	148	21	169
Negative	45	479	524
Total	193	500	693
	76.7%	95.8%	90.5%
	Sensitivity	**Specificity**	**Agreement**
Lower Confidence Interval	**71%**	**94%**	**88%**
Upper Confidence Interval	**83%**	**98%**	**93%**
Allergens included: nOle e 1, nArt v 1, Dog Serum Albumin (Can f 3), nBet v 1, and Cat Serum Albumin (Fel d 2).			

IMMULITE® 2000 3gAllergy™ assay results for all allergens compare well with clinical documentation of presence or absence of signs, symptoms and other diagnostic evidence of allergen sensitivity

Conclusions for all Studies

Allergens including nOle e 1, nArt v 1, Dog Serum Albumin (Can f 3), nBet v 1 and Cat Serum Albumin (Fel d 2) for use with the IMMULITE® 2000 3gAllergy Specific IgE assay demonstrate acceptable analytical performance including precision, linearity and specificity. IMMULITE® 2000 assay results compare well with clinical documentation of presence or absence of signs, symptoms and other diagnostic evidence of allergen sensitivity. Substantial equivalence was demonstrated to clinical data, supporting the following intended use of the IMMULITE® 2000 3gAllergys Specific IgE assay and the five previously listed allergens:

> For *in vitro* diagnostic use with the IMMULITE® 2000 Analyzer — for the quantitative measurement of allergen-specific IgE in human serum, as an aid in the clinical diagnosis of IgE-mediated allergic disorders. The test results are to be used in conjunction with clinical findings and other laboratory tests.

As per 21 CFR 807.92(b)(3) the tests conducted for the IMMULITE® 2000 3gAllergy Specific IgE assay demonstrates that the device is substantially equivalent and safe and effective and performs as well as the predicate device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Siemens Healthcare Diagnostics, Inc.
c/o Mr. Garo Mimaryan
Technical Regulatory Affairs Specialist III
511 Benedict Avenue
Tarrytown, NY 10591

JAN 0 6 2012

Re: k112523
Trade/Device Name: IMMULITE® 2000 3gAllergy™ Specific IgE Assay Kit
Regulation Number: 21 CFR §866.5750
Regulation Name: Radioallergosorbent (RAST) immunological test system
Regulatory Class: Class II
Product Code: DHB
Dated: January 4, 2012
Received: January 5, 2012

Dear Mr. Mimaryan:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed

predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Office of *In Vitro* Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): K112523

Device Name: IMMULITE® 2000 3gAllergy™ Specific IgE Assay

Indication For Use:

For *in vitro* diagnostic use with the IMMULITE 2000 Analyzer — for the quantitative measurement of allergen-specific IgE in human serum, as an aid in the clinical diagnosis of IgE-mediated allergic disorders. The test results are to be used in conjunction with clinical findings and other laboratory tests.

Prescription Use ___√___ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Maria M Chan

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K112523